REMARKS

Status of the Claims

Claims 1-11, 19, and 22-29 are pending in the present application. Claims 1 and 22-23 have been amended to specify that the variants encompassed encode a polypeptide having at least 95% sequence identity to SEQ ID NO:3 or 5. Support for this amendment can be found, for example, on page 17, lines 15-18 of the instant specification. Claims 1 and 22-23 have also been amended to recite that the pesticidal activity is against lepidopteran pests. Support for this amendment can be found, for example, in Experimental Example 8. No new matter has been added by way of this amendment. Claims 24-29 have been canceled due to the amendment of claims 1 and 22-23. Claims 1-11, 19, and 22-23 are pending.

The Rejections Under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Enablement

The Examiner maintained the rejection of claims 1-11, 19 and 22-26 under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable one skilled in the art to make or use the invention. The Examiner asserts that the specification, while enabling for nucleic acids encoding SEQ ID NO:3 or 5, host cells, plants, plant cells and seeds comprising them, and a method of using them to make SEQ ID NO:3 or 5, does not reasonably provide enablement for methods and compositions drawn to nucleic acids encoding pesticidal proteins with 90% or 95% sequence identity to SEQ ID NO:3 or 5, nucleic acids with 90% or 95% identity to SEQ ID NO:1, 2, or 4, or host cells, plants, plant cells and seeds comprising them, and a method of using them to make a pesticidal protein with 90% or 95% identity to SEQ ID NO:1, 2, or 4.

Applicants respectfully traverse this rejection for the reasons of record. However, to expedite prosecution, claims 1 and 22-23 have been amended to specify that the variants encompassed encode a polypeptide having at least 95% sequence identity to SEQ ID NO:3 or 5 wherein the variants have pesticidal activity against lepidopteran pests. Claims 24-29 have been

canceled. In view of these amendments, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

Written Description

Claims 1-11, 19, and 22-29 were further rejected under 35 U.S.C. § 112, first paragraph, as failing to satisfy the written description requirement. The rejection is respectfully traversed.

The Examiner asserts that the disclosure is insufficient to support claims that are drawn to a genus of nucleic acids having 90% or 95% sequence identity to SEQ ID NO:1, 2, or 4, or nucleic acids encoding polypeptides having 90% or 95% identity to SEQ ID NO:3 or 5. Applicants respectfully traverse this rejection for the reasons of record. However, to expedite prosecution, claims 1 and 22-23 have been amended to specify that the variants encompassed encode a polypeptide having at least 95% sequence identity to SEQ ID NO:3 or 5 wherein the polypeptide has pesticidal activity against lepidopteran pests. Claims 24-29 have been canceled. In view of these amendments, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for failing to satisfy the written description requirement.

The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn

The Examiner has rejected claims 1, 4-7, 24 and 27 under 35 U.S.C. § 103(a) as being unpatentable over Ben-Dov *et al.* (1996) *Appl. Environ. Microbiol.* 62:3140-3145 in view of Carlton *et al.* (1985) Mol. Biol. Microb. Differ., Proc. Intl. Spore Conf., 9th, Meeting date 1984, pages 246-252, and claims 2-3, 8-11, 19, 22-23, 25-26, and 28-29 under 35 U.S.C. § 103(a) as being unpatentable over Ben-Dov *et al.* in view of Carlton *et al.* and Koziel *et al.* (U.S. Patent 5,625,136). Claims 24-29 have been canceled. The rejection of claims 1-11, 19 and 22-23 is respectfully traversed.

Ben-Dov *et al.* teach cloning of large restriction fragments from *Bacillus thuringiensis* subsp. *israelensis* and identification of known toxins using Southern hybridization and probes specific for the known toxins. Carlton *et al.* teach that *Bacillus thuringiensis* strain HD536 has a 68 MDa plasmid implicated in toxin production. The Examiner suggests that at the time the invention was made it would be obvious to one of ordinary skill in the art to modify the method

of cloning delta-endotoxin genes as taught by Ben-Dov *et al.* to clone delta-endotoxin genes from strain HD536 described in Carlton *et al.* The Examiner also states that one of ordinary skill in the art would have been motivated to do so because an increased repertoire of delta-endotoxins would be desirable for increasing toxicity spectra and for overcoming pest resistance to the existing endotoxins. Finally, the Examiner suggests that one of skill in the art would necessarily isolate a nucleic acid encoding SEQ ID NO:3 or 5 when cloning toxins from HD536. The Applicants respectfully disagree.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385 (U.S. 2007). In the instant invention, Applicants contend that there would be no reasonable expectation of success in isolating the AXMI-014 sequences encompassed therein. For that matter, there was no reasonable expectation of success in obtaining any toxin genes from HD536 since no insecticidal activity was demonstrated for this strain prior to the Applicant's disclosure. The evidence described was that when the ~68 MDa plasmid was present the strain was cry+, meaning it has a crystal protein presumably at sporulation, and when the strain was "cured" of the plasmid, meaning the strain was treated so that the plasmid was absent from derived strain, then the strain was cry- , meaning no crystal protein was present in the strain. Additionally, when the ~68 MD plasmid was transferred to a cry- *B. thuringiensis* strain or *B. cereus* strain the recipient strain was converted to cry+. The presence of a crystal protein provides no evidence for the presence of a gene or encoded protein having insecticidal activity against any pest, let alone lepidopteran pests.

Furthermore, AXMI-014 has low sequence homology with other known toxins (<30%), thus one of skill could not have used the cryIVA, cryIVB, cryIVC, cryIVD, and cytA, probes disclosed in Ben-Dov *et al.* to isolate SEQ ID NO:1, 2, or 4 from HD536. In fact, only the cryIVA probe was able to detect any gene other than itself, and the authors attribute this cross-reactivity with the degree of sequence homology between the two genes (see column 2, page 3143 of Ben-Dov *et al.*). Thus, it is not clear how one of skill in the art would be able to use the hybridization method disclosed by Ben-Dov *et al.* to isolate the sequences of the invention.

The Federal Circuit has recently affirmed this line of reasoning in *Eisai Co. Ltd. V. Dr. Reddy's Laboratories, Ltd. and Teva Pharmaceuticals USA, Inc.,* No. 2007-1397, 2007-1398 (Fed. Cir. 2008), which was decided after both *KSR* and *Kubin*, by finding that a chemical structure (e.g., a polynucleotide or polypeptide) cannot be considered obvious unless the prior art suggests a lead compound *and modifications necessary to achieve the claimed molecule*. In *Eisai*, Teva asserted that a combination of three prior art references rendered the claims of the '552 patent to rabeprazole and its salts obvious. The prior art references teach the compound lansoprazole, which differs from rabeprazole solely in the substituent at the 4th position of the pyridine ring. Teva argued that lansoprazole would have been selected by a person of ordinary skill in the art as a lead compound that could have been modified to produce rabeprazole. The Federal Circuit found that there existed no reason to substitute the fluorinated substituent of lansoprazole for the methoxypropoxy substituent of rabeprazole. In making this conclusion, the Federal Circuit stated that "KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound," (emphasis added) citing *Takeda* 492 F.3d at 1357. The Federal Circuit further states "obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e., a lead compound) in a particular way to achieve the claimed compound" *Eisai*, emphasis added. As there is no structural similarity between the known cry toxins identified by Ben-Dov *et al.* and the AXMI-014 protein disclosed in the instant specification, it would not have been obvious to use the methods disclosed by Ben-Dov to isolate the sequences of the instant invention from a strain that was not known to have pesticidal activity.

In view of the above remarks, Applicants respectfully request that the rejection of claims 1, 4-7, and 20 under 35 U.S.C. § 103(a) be withdrawn.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of

this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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